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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,288	11/28/2000	Dale B. Schenk	15270J-004765US	9431

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/724,288	SCHENK ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *92,97,98 and 100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *92,97,98 and 100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 21 December 2007 have been entered. Claims 92, 97, 98, and 100 are pending and under examination.

2. The indicated allowability of claims 92, 97, 98, and 100 is withdrawn in view of the newly discovered reference(s) to Ulvestad, Selkoe, and Wong. Rejections based on the newly cited reference(s) follow.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 92, 97, and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ard (1996. Journal of Neuroscience Research 43:190-202, cited in previous office action) in view of Ulvestad (1994. Journal of Neuropathology and Experimental Neurology 53:27-36).

Ard teaches methods of contacting amyloid deposits with serum, which comprises antibodies, and adding the composition (i.e., both the amyloid deposit and the antibodies together) to microglial cells. This is a screening method and is on point to claims 92 and 97. Ard teaches that cultured microglia have the ability to clear Aβ peptide (see abstract, see also Figure 1) and teaches contacting Aβ with microglia, followed by a series of measurements to determine whether a reduction in the amount of amyloid deposit occurs; see p. 196 and Figures 6 – 9). Ard teaches that microglia are capable of removing Aβ peptide from solutions (see p.

199 top of second column). Ard also teaches methods comprising contacting Aβ (amyloid) deposits with microglia and measuring the amount of Aβ taken up by microglia, wherein the Aβ deposit is a tissue sample from the brain of an Alzheimer's patient (see p. 196 final paragraph - p. 199), which is on point to claim 100. However Ard does not explicitly teach combining the amyloid deposit with the antibody prior to adding microglial cells as recited in claim 92 and does not explicitly teach screening monoclonal antibodies as recited in claims 97 and 100.

Ulvestad teaches that microglia have Fc receptors on their surface, which is on point to claims 92, 97, and 100. Ulvestead also teaches that when contacted with immune complexes comprising antibodies bound to their cognate antigen, Fc receptors on microglia become active and the microglia phagocytose their targets (see abstract, see also p. 34 first column final paragraph and p. 34 second column first complete paragraph). Ulvestad teaches contacting antibodies and their antigen (here, erythrocytes and antibodies, referred to as EA) with one another prior to contacting them with microglia (p. 29, phagocytosis assay). The reference indicates that phagocytosis of antigen by microglia occurs if intact antibodies are contacted with their antigen, but not when F(ab')2 fragments are used (p. 31, second column). This indicates that Fc receptors must be activated by the antigen-antibody complex in order for phagocytosis to occur, as F(ab')2 fragments lack the Fc region and cannot activate Fc receptors. Finally, Ulvestad teaches that monoclonal antibodies can be used in such assays (p. 28, paragraph spanning the two columns), which is on point to claims 97 and 100. However Ulvestad does not teach contacting samples comprising amyloid deposits with microglia.

It would have been obvious to one of ordinary skill in the art to modify the methods of Ard by contacting the samples comprising amyloid deposits with antibodies prior to adding microglia, as suggested by Ulvestad, with a reasonable expectation of success. The motivation to do so would be to activate the Fc receptors on the microglia, which Ulvestad teaches is a necessary step in activating the phagocytic activity of these cells and would be required to successfully identify antibodies that bind to Aβ amyloid deposits and are subsequently phagocytosed by microglia. As Ard is on point to measuring the amount of Aβ taken up by microglia, it would have been obvious to one of ordinary skill in the art to modify the method in this manner, thereby arriving at the invention of claim 92.

Additionally, it would have been obvious to one of ordinary skill in the art to modify the method of Ard by including monoclonal antibodies, as taught by Ulvestad, thereby arriving at the inventions of claims 97 and 100. Doing so would have been obvious, as Ulvestad teaches that

such monoclonals can be used to activate microglia, since monoclonals have an intact Fc region.

4. Claims 92, 97 – 98, and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ard in view of Ulvestad as applied to claims 92, 97, and 100 above, and further in view of Wong (1985. Proc Natl Acad Sci USA 82:8729-8732) and Selkoe (U.S. Patent 5,262,332).

The reasons why claims 92, 97, and 100 are obvious over Ard in view of Ulvestad are set forth in the previous rejection. However none of the references teaches antibodies that bind to residues 1 – 7 of Aβ as recited in claim 98.

Wong teaches that antibodies raised against the N-terminus of Aβ peptide, particularly residues 1 – 10, tightly bind to plaques found in Alzheimer's disease tissue. This is relevant to the limitation recited in claim 98, drawn to antibodies that bind to epitopes within residues 1 – 7 of Aβ, although this teaching does not explicitly indicate the location of the eptiope bound. However Wong does not teach contacting amyloid deposits with microglia as encompassed by claims 92, 97 – 98, and 100, and does not explicitly teach antibodies that bind to an epitope within residues 1 – 7 of Aβ as recited in claim 98.

Selkoe teaches antibodies that bind to "about 8 or more" consecutive residues of Aβ protein. Seven is about 8, so the reference is on point to the limitation recited in claim 98, i.e. antibodies that bind to epitopes within residues 1 – 7 of Aβ. Selkoe teaches that such antibodies, raised against even a very small fragment of the Aβ peptide, can be used in diagnostic assays for Alzheimer's disease (column 5). However Selkoe does not teach contacting amyloid deposits with microglia as encompassed by claims 92, 97 – 98, and 100 and does not explicitly point to the first 7 amino acids of Aβ peptide as those containing the most appropriate epitope.

It would have been obvious to one of ordinary skill in the art to select an antibody that binds to an epitope within residues 1 – 7 of Aβ, for use in the screening assays, thereby arriving at the invention of claim 98. The motivation to do so would be to select use an antibody that binds tightly to Aβ, allowing for the microglia to take up this protein. Wong points to the first 10 amino acids as appropriate targets for antibodies, and notes that antibodies raised against this region bind to Aβ. Additionally, Selkoe provides the artisan of ordinary skill with a reasonable expectation of success in using antibodies that are raised against "about 8", i.e. seven

consecutive amino acids. Selkoe guides the artisan to select the first seven residues of Aβ peptide as those to which an antibody should bind.

Conclusion

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker, Ph.D./
Patent Examiner, Art Unit 1649
March 3, 2008

/Robert C. Hayes, Ph.D./
Primary Examiner, Art Unit 1649